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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Janice A. Vatland
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, MA 02210

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

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11/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,755	STAHL ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13,15-17,22-33,35-38,40-51,53-62 and 67-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-13,15-17,22-33,35-38,40-51,53-62 and 67-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/01/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/01/2010, is acknowledged.

2. Claims 1, 3-13, 15-17, 22-33, 35-38, 40-51, 53-62 and 67-74 are pending and under examination in the instant application.

3. Applicant's IDS, filed 04/30/2010, is acknowledged.

4. In view of the amendment filed on 11/01/2010, only the following rejections are remained.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 12 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The "mammalian cell with a surface exposed MBL ligand" recited in claim 12 has no antecedent basis in base claim 1.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that it would be clear to one of ordinary skill in the art based on the plain language of the claims and the teachings provided in the specification that the antecedent baseis for claim 12 is derived from the administering step of claim 1.

However, in base claim 1, the contact interaction between the MBL inhibitor and its target ligand is not limited to mammalian cell. Base claim 1 is not limited to mammalian cell but read on contact interaction that can occur in cerebrospinal fluid, plasma or serum.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 3-13, 15-17, 22-33, 35-38, 40-51, 53-62 and 67-74 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicants point that the specification provides a sufficient description of the MBL inhibitors of the claims. For example, the specification describes, on page 3, lines 23-27, MBL-binding peptides that have a MBL-binding CDR3 region and provides that MBL-binding peptides can be antibodies or antibody fragments. On page 4, line 24 through page 5, line 24, the specification again teaches that MBL-binding peptides can have a CDR3 from the three deposited antibodies, and that the MBL-binding peptides can be intact soluble monoclonal antibodies, humanized antibodies or antibody fragments. On page 18, lines 28-31, the instant specification teaches that the CDR regions, and in particular the CDR3 region, can be incorporated into other antibodies. Further, humanized monoclonal antibodies that contain a CDR3 region from the deposited antibodies are provided on page 21, line 4 through page 23, line 2. Antibody fragments, including humanized monoclonal antibody fragments are described on page 25, line 3 through page 26, line 29. Applicant submits that the instant specification also teaches that several peptides which bind to MBL or MASP have been described in the art, including Lanzrein, A.S. et al., "Mannan-binding lectin in human serum, cerebrospinal fluid and brain tissue and its role in Alzheimer's disease", Department of Pharmacology, University of Oxford, UK, May 11, 1998, Neuroreport, 9(7):1491-5; Jack, D.L. et al., "Activation of complement by mannose-binding lectin on isogenic mutants of Neisseria meningitidis serogroup B", lmmunobiology Unit, Institute of Child Health, London, UK, J Immunol, February 1, 1998,160(3): 1346-53, Terai, I. et al., "Human serum mannose-binding lectin (MBL)-as sociated serine protease- 1 (MASP- 1): determination of levels in body fluids and identification of two forms in serum", Division of Clinical Pathology, Hokkaido Institute of Public Health, Sapporo, Japan, Clin. Exp. Immunol., Nov., 1997, 110(2):317-23; Endo, M. et al., "Glomerular deposition of mannose-binding lectin (MBL) indicates a novel mechanism of complement activation in IgA nephropathy [In Process Citation]", Second Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan, Nephrol Dial Transplant, August 13, 1998, (8): 1984-90; Valdimarsson, H. et al., "Reconstitution of opsonizing activity by infusion of mannan-binding lectin (MBL) to MBL-deficient humans", Department of Immunology, University of Reykjavik, Iceland, Scand. J. Immunol., August 1998, 48(2):116-23; and Thiel, S. et al., "The concentration of the C-type lectin, mannan-binding protein, in human plasma increases during an acute phase response", Clin Exp. Immunol., Oct. 1992, 90(1):31-5. With at least the above-described support found in the instant specification, one of ordinary skill in the art would clearly recognize a description of the claimed subject matter, and, therefore, the instant disclosure adequately describes the claimed invention such that one of ordinary skill in the art would recognize that Applicant, at that time the instant application was filed, had possession of the claimed invention.

However, the specification provides only generic terms for the inhibitor. No correlation in the specification between the MBL-binding CDR3 region and its function to bind to "mammalian

cell with a surface exposed MBL ligand", "binds to MBL", "binds to a human MBL epitope", "inhibits VCAM-1 expression" and "binds to MASP or mannan". One of skill in the art would not envisage, based on the instant disclosure, the claimed genus of peptides, proteins, antibodies, and antigen-binding fragment thereof which retain the features essential to the instant invention. With respect to the cited references the Examiner notes the following:

Lanzrein et al dose not teach any peptide that binds to MBL or MASP.

Jack et al, teach only carbohydrate ligand *N*-acetyl-glucosamine which binds to MBL but no peptides.

Terai et al teaches α2-macroglobulin has been found to bind to MASP and to inhibit its proteolytic action, no peptides.

Endo et al teach no peptides that bind to MBL or MASP.

Valdimarsson, H. et al no peptides that bind to MBL or MASP.

Thiel et al teach Mannose and GlcNAc were the most efficient inhibitors of the binding MBP.

Again, neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (a peptide, protein, or antibody or antigen-binding fragment thereof) to describe the claimed genus, nor does it provide a description of structural features that are common to species (a peptide, protein, or antibody or antigen-binding fragment thereof). The specification provides no structural description of a peptide, protein, or antibody or antigen-binding fragment thereof other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed a peptide, protein, or antibody or antigen-binding fragment thereof looks like. The specification's disclosure is inadequate to describe the claimed genus of a peptide, protein, or antibody or antigen-binding fragment thereof.

9. Claims 1, 3-13, 15-17, 22-33, 35-38, 40-51, 53-62 and 67-74 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that all but the cited Collard et al. reference are not relevant to the claimed methods for inhibiting LCP complement activation. From these references, therefore, it is not reasonable to doubt Applicant' s teachings and to draw a negative conclusion in regard to the enablement of the specifically claimed methods. Second, Applicant respectfully wishes to bring to the Examiner's attention that the cited Collard et al. reference describes the inventors' own work and demonstrates that the inventors generated three monoclonal antibodies that "were very potent inhibitors of MBL deposition after endothelial oxidative stress" (as stated in the second to last paragraph of the article.) Finally, even if the claims encompass yet to be identified inhibitors, such is not the standard by which to challenge enablement. Accordingly, based on the teachings provided in the instant specification and the level of skill of those of ordinary skill in the art, one of ordinary skill would need use only routine experimentation to practice the claimed methods, and the Examiner has not established otherwise.

However, while applicant did not dispute the facts in the cited references, applicant dismisses the teachings of these references as “not relevant”. For example, it is not clear why Stanworth et al (British Jounal of Rheumatology, 1998, 57:186-188) teachings are “not relevant”. Sanworth et al teach that no evidence was found to support an association between the presence of MBL allele and protection from rheumatoid disease, genotype frequencies were similar in both groups. This suggests that complement activation via MBL-aglactosyl IgG complexes is unlikely to play a major role in the pathophysiology of RA (see abstract in particular). The Examiner maintains that all cited references are relevant to the rejection of record.

It appears that applicant admits that only three monoclonal antibodies that "were very potent inhibitors of MBL deposition after endothelial oxidative stress" are disclosed but no peptides, proteins are known as MBL inhibitors.

It remains the Examiner’s position that Applicant has not provided sufficient biochemical information that distinctly identifies MBL inhibitor such as any “peptide, protein, or antibody or antigen-binding fragment thereof” that binds to “mammalian cell with a surface exposed MBL ligand”, “binds to MBL", "binds to a human MBL epitope", "inhibits VCAM-1 expression" and "binds to MASP or mannan". While any MBL inhibitor may have some notion of the activity of the “inhibitory agent”, claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. The specification fails to provide any guidance on how to make any MBL inhibitor peptide, protein, antibody that can be used to inhibit adhesion cellular injury in a subject.

Given the relatively incomplete understanding in correlating *in vitro* assays and *in vivo* animal models to clinical treatment of lectin complement pathway associated complement activation mediates a cellular/tissue injury involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims, the claims are not enabled. See MPEP 2164.08.

If the use disclosed is of such nature that the art is unaware of successful treatments with chemically analogous compounds, a more complete statement of how to use must be supplied. "The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements...However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims." MPEP § 2164.03.

"Substantiating evidence may be in the form of animal tests which constitute recognized screening procedures with clear relevance to utility in humans. See *Ex parte Krepelka*, 231 USPQ 746 (Board of Patent Appeals and Interferences 1986) and cases cited therein." *Ex parte Maas*, 9 USPQ2d 1746.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 12, 30-33, 38, 40, 50, 51, 56 and 60-62 stand rejected under 35 U.S.C. 102(b) as being anticipated by US. Pat. No. 5,270,199 (IDS reference A1) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that in order to be inherently anticipated the recited prior art must necessarily achieve the claimed invention each and every time the recited prior art is practiced. The Examiner has failed to establish that this is the case. The Examiner merely states that the MBP protein would bind to MASP in the absence of evidence to the contrary. However, the Examiner is respectfully reminded that the claims are directed to a method for inhibiting lectin complement pathway (LCP) associated complement activation mediated cellular injury. Therefore, it must be established that the practice of the prior art would necessarily achieve such inhibition each and every time the prior art is practiced.

However, regarding process claims, a preamble recitation that merely expresses the purpose of performing the claimed steps is not a limitation on the process where the body of the claim fully sets forth the steps required to practice the claimed process, and where the preamble recitation

does not affect how the claimed steps are to be performed. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001).

Thus, in *Bristol-Myers*, the court held that preamble language stating that a treatment method was "for reducing hematologic toxicity" did not limit the claim since the steps would be "performed in the same way regardless whether or not the patient experiences a reduction in hematologic toxicity, and the language of the claim itself strongly suggests the independence of the preamble from the body of the claim." *Id.* at 1375. The *Bristol-Myers* court similarly held that preamble language reciting "[a] method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity" did not limit the treatment method claim because it was "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim." *Id.* at 1375-76.

In the instant case, preamble language in claims of the instant application directed to "inhibiting lectin complement pathway (LCP) associated complement activation" are expressions of purposes and intended results, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. In re Hirao 190 USPQ 15, 16-17, (CCPA 1976) held that the preamble was non-limiting because it merely recited the purpose of the process, which was fully set forth in the body of the claim.

12. Claims 1, 12, 30-33, 38, 40, 50, 51, 56 and 60-62 stand rejected under 35 U.S.C. 102(b) as being anticipated by Fischer et al (Scand. J. Immunol. 39,439-445, 1994) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that in order to establish inherent anticipation the recited prior art must necessarily achieve the claimed invention each and every time the recited prior art is practiced. The Examiner has not demonstrated that this is the case. The Examiner has tried to argue that Fischer et al. teach the administration to the same subjects of the claims, but has not offered any evidence outside of his opinion as to why this is the case.

However, regarding process claims, a preamble recitation that merely expresses the purpose of performing the claimed steps is not a limitation on the process where the body of the claim fully sets forth the steps required to practice the claimed process, and where the preamble recitation does not affect how the claimed steps are to be performed. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001).

Thus, in *Bristol-Myers*, the court held that preamble language stating that a treatment method was "for reducing hematologic toxicity" did not limit the claim since the steps would be

"performed in the same way regardless whether or not the patient experiences a reduction in hematologic toxicity, and the language of the claim itself strongly suggests the independence of the preamble from the body of the claim." *Id.* at 1375. The *Bristol-Myers* court similarly held that preamble language reciting "[a] method for treating a cancer patient to effect regression of a taxol-sensitive tumor, said method being associated with reduced hematologic toxicity" did not limit the treatment method claim because it was "only a statement of purpose and intended result. The expression does not result in a manipulative difference in the steps of the claim." *Id.* at 1375-76.

In the instant case, preamble language in claims of the instant application directed to "inhibiting lectin complement pathway (LCP) associated complement activation" are expressions of purposes and intended results, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. In re Hirao 190 USPQ 15, 16-17, (CCPA 1976) held that the preamble was non-limiting because it merely recited the purpose of the process, which was fully set forth in the body of the claim.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 6, 12, 13, 15, 25, 26, 30-33, 35, 38, 40, 44, 50, 51, 53, 56, 57, 60-63, 70-71 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Endo et al (Nephrol Dial Transplant. 1998 Aug;13(8):1984-90, IDS C13) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that the Examiner has not demonstrated that the teachings of Endo et al. teach or suggest the administration of an MBL inhibitor to a subject with a cellular injury to inhibit

LCP complement activation mediated cellular injury. Without such a demonstration this rejection cannot be maintained.

However, it is the Examiner's position that base on the observation in Endo et al that glomerular deposition of MBL, which was accompanied by MASP-1, in association with C3b/C3c and C5b-9, indicates complement activation in IgA nephropathy. This suggests that lectin pathway participates in the development of the IgA nephropathy disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made would be motivated to therapeutic target the formation of MBL/MASPs complex taught by Endo et al with MBL inhibitor such as monoclonal antibodies against MBL or MASP-1 taught by Endo et al for the treatment/inhibition the initiation of MBL/MASPs complex and prevent the development of glomerular injury. One of ordinary skill in the art would have had a reasonable expectation of success of inhibiting LCP associated complement activation mediated IgA nephropathy according to the teachings of Endo et al by providing an anti-MBL antibody or anti-MASP-1 to a patient suffering from this disease inasmuch as the reference discloses that the lectin pathway is initiated intermittently by MBL/MASPs complex and serves as a trigger for the activation of the amplification cycle via the alternative pathway and that this initiation is associated with repeated antigen exposures such as infection and it discloses specific examples of such anti-MBL antibodies and anti-MASPs antibodies.

15. Claims 1, 6, 12, 13, 15, 25, 26, 30-33, 35, 38, 40, 44, 50, 51, 53, 56, 57, 60-63, 70-71 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Malhotra et al (Nat Med. 1995 (3):237-43) in view of Endo et al (Nephrol Dial Transplant. 1998 Aug;13(8):1984-90, IDS C13) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that the Examiner has not demonstrated that Endo et al. teach or suggest the administration of an MBL inhibitor to a subject with a cellular injury to inhibit LCP complement activation mediated cellular injury. As this rejection relies on Endo et al., this rejection cannot be maintained.

However, it remains the Examiner's position that base on the observation that the occurrence of MBP in synovial fluid coupled with the presence of high levels of IgG-G0 structures leading to generation of inflammatory response of the synovial membrane of affected joints. This suggests that lectin pathway participates in the development of rheumatoid arthritis. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made would be motivated to therapeutic target the formation of MBL/IgG0 complex taught by Malhotra et al with MBL inhibitor such as monoclonal antibodies against MBL taught by Endo et al for the treatment/inhibition the initiation of MBL/IgG0 complex and prevent the development of rheumatoid arthritis. One of ordinary skill in the art would have had a reasonable expectation of success of inhibiting LCP associated complement activation mediated

rheumatoid arthritis according to the teachings of Malhotra et al by providing an anti-MBL antibody or anti-MASP-1 taught by Endo et al to a patient suffering from rheumatoid arthritis disease inasmuch as the Malhotra reference discloses that the lectin pathway is initiated by MBL/IgG0 complex results in activation of the complement that contributes to the chronic inflammation of the synovial membrane, which arise from the localization (deposition) of the IgG-G0 on the affected joint from the resulting activation of complement and it discloses specific examples of such anti-MBL antibodies and anti-MASPs antibodies.

16. Claims 1, 6, 12, 13, 15, 25, 26, 30-33, 35, 38, 40, 44, 50, 51, 53, 56, 57, 60-63, 70-71 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuda et al., (Joumal of Nephrology Association of Japan, 39(3): 235 (1997)), optionally in view of Endo et al (Nephrol Dial Transplant. 1998 Aug;13(8):1984-90, IDS C13) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that the Examiner has not demonstrated that either Matsuda et al. or Endo et al. teach or suggest the administration of an MBL inhibitor to a subject with a cellular injury to inhibit LCP complement activation mediated cellular injury. Accordingly, this rejection cannot be maintained.

However, the Examiner's position remains that base on the observation that tendency of higher renal dysfunction was observed in MBP-positive cases, and higher frequenceies of C2 and C4 staining in glomerulus were found in MBP-positve compared to MBP-negative patients with IgA nephropathy. This suggests that involvement of MBP in incidence and development of IgA nephropathy. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made would be motivated to therapeutic target MBP taught by Matsuda et al with MBL inhibitor such as monoclonal antibodies against MBL taught by Matsuda et al or Endo et al for the treatment/inhibition of MBPand prevent the development of IgA nephropathy. One of ordinary skill in the art would have had a reasonable expectation of success of inhibiting LCP associated complement activation mediated IgA nephropathy according to the teachings of Matsuda et al by providing an anti-MBL antibody or anti-MASP-1 taught by Matsuda et al or Endo et al to a patient suffering from IgA nephropathy disease inasmuch as the Matsuda reference discloses that the tendency of higher renal dysfunction was observed in MBP-positive cases and it discloses specific examples of such anti-MBL antibodies.

17. Claims 22-23, 25-26, 28-29, 36-37, 54-5567-68 and 73-74 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Endo et al (Nephrol Dial Transplant. 1998 Aug;13(8):1984-90, IDS C13) as applied to claims 1, 13, 33, 40, 51 and 70 and further in view of Owens et al (1994) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant argues that the Examiner has not demonstrated that Endo et al. teach or suggest the administration of an MBL inhibitor to a subject with a cellular injury to inhibit LCP complement activation mediated cellular injury. As this rejection relies on Endo et al., this rejection cannot be maintained.

However, the Examiner's position remains that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the antibody taught by Endo et al as humanized antibody, Fab and $F(ab')_2$ fragments taught by the Owens et al. because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications as taught by Owens *et al.*

18. Claims 22-23, 25-26, 28-29, 36-37, 54-5567-68 and 73-74 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Malhotra et al (Nat Med. 1995 (3):237-43) in view of Endo et al (Nephrol Dial Transplant. 1998 Aug;13(8):1984-90, IDS C13) as applied to claims 1, 13, 33, 40, 51 and 70 and further in view of Owens et al (1994) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant submits that the Examiner has not demonstrated that Endo et al. teach or suggest the administration of an MBL inhibitor to a subject with a cellular injury to inhibit LCP complement activation mediated cellular injury. As this rejection relies on Endo et al., this rejection cannot be maintained.

However, it remains the Examiner's position that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce the antibody taught by Endo et al as humanized antibody, Fab and $F(ab')_2$ fragments taught by the Owens *et al*. because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications as taught by Owens *et al.*

18. Claims 22-23, 25-26, 28-29, 36-37, 54-5567-68 and 73-74 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuda et al., (Joumal of Nephrology Association of Japan, 39(3): 235 (1997)), optionally in view of Endo et al (Nephrol Dial Transplant. 1998 Aug;13(8):1984-90, IDS C13), as applied to claims 1, 13, 33, 40, 51 and 70 and further in view of Owens *et al* (1994) for the same reasons set forth in the previous Office Action mailed 04/30/2010.

Applicant's arguments, filed 11/01/2010, have been fully considered, but have not been found convincing.

Applicant argues that the Examiner has not demonstrated that either Matsuda et al. or Endo et al. teach or suggest the administration of an MBL inhibitor to a subject with a cellular injury to inhibit LCP complement activation mediated cellular injury. As this rejection relies on Matsuda et al. or Endo et al., this rejection cannot be maintained.

However, it is the Examiner's position that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce the antibody taught by Matsuda et al or Endo et al as humanized antibody, Fab and $F(ab')_2$ fragments taught by the Owens *et al*. because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications as taught by Owens *et al*.

19. No claim is allowed.

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
November 4, 2010

/Maher M. Haddad/
Primary Examiner
Technology Center 1600